Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 26 claims. Claims 3-5 and 14-26 were cancelled as the result of a restriction requirement. Claim 10 has been cancelled herein. Thus, the claims presently pending in the application are 1, 2, 6-9, and 11-13.

II. The Amendments

Claim 1 was amended to eliminate the transitional phrase "consisting functionally of" and to replace the phrase "except as existing in nature" with "substantially purified." Support for this amendment may be found on page 2 of the application, lines 1-3. A definition for "substantially pure" may be found on page 5 of the application, line 23-page 6, line 2.

Claim 6 was amended to replace the phrase "except as existing in nature" with the phrase "substantially purified." Support may be found in the same sections discussed above in connection with claim 1. In addition, claim 6 was made dependent upon claim 1.

The specification of the application was amended on page 6 to eliminate a typographical error pointed out by the Examiner.

None of the amendments discussed above add new matter to the application and their entry is therefore respectfully requested.

III. Objections to the Specification and Claims

On page 3 of the Office Action, the Examiner objects to the use of the term "R1C3 receptor protein" on page 6 of the application, line 21. As suggested, the term represented a typographical error and has now been replaced with "B1C3 receptor protein."

The Examiner also objects to claim 10 but since this has now been cancelled, the objection has been obviated.

The Rejections

I. Rejection of Claims Under 35 U.S.C. § 101

On pages 3-7 of the Office Action, the Examiner rejects all pending claims under 35 U.S.C. § 101 based upon the allegation that the application fails to provide a credible utility for the claimed invention.

Applicants respectfully traverse this rejection.

First, Applicants would like to point out that the B1C3 protein has been characterized by others. In particular, Glickman, *et al.* cloned the same gene from rat and showed that it is highly expressed in the brain (*Mol. Cell Neurosci. 14*:141-152 (1999); cited as document AN1 in Applicants' IDS of March 27, 2003). Im, *et al.* also cloned the same gene (referred to as edg-a) and showed it is highly expressed in the rat spleen and brain and that it functions as a sphingosine-1-phosphate responsive GPCR (*J. Biol. Chem. 275*:14281-14286 (2000), cited as document AP1 in Applicants' IDS of March 27, 2003). However, even in the absence of these the publications, Applicants believe that the utility requirement has been met for the B1C3 receptor claimed.

Patent law requires that an application assert a utility for a claimed invention which is substantial, specific and credible. As recognized by the Examiner, the present application asserts that the B1C3 receptor may be used in assays for the purpose of identifying new analgesic drug candidates. Thus, a utility has been asserted in the specification that is clearly both specific (not all proteins can be used in assays for identifying such potential analgesics) and substantial (the identification of potential new therapeutic agents based upon *in vitro* assays has been specifically recognized by the Patent Office in its utility guidelines as being sufficient to support patentability). As discussed in MPEP § 2107, *et seq.*, once a utility that is specific and substantial has been asserted in an application the only remaining basis for rejecting claims is that the asserted utility is not credible.

In order to be credible, it is not necessary for an applicant to show that an invention works with absolute certainty and the requirements of patentability can be met even though considerable

further research and development is needed before an invention can be used for its asserted purpose (see *In re Brana*, 51 F.3d 1560 (1995) cited in MPEP). The relevant test for credibility is set forth in the Manual as follows:

> An assertion is credible unless (a) the logic underlying the assertion is seriously flawed or (b) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion.[1]

The overall reasoning underlying Applicants' asserted utility is as follows: (a) a G protein-coupled receptor was isolated from a rat brain cDNA library (see page 14 of the application, line 1-page 15, line 10; page 15, line 12-page 16, line 14); (b) G protein-coupled receptors located in the central nervous system are known to be involved in the transmission, modulation and sensation of pain (see page 1 of the specification, lines 15-20); (c) *in situ* hybridization studies have indicated that the receptor is preferentially and ubiquitously expressed in specific structures within regions of the brain (a lesser amount of B1C3 was expressed in the spleen and no expression was detected in the heart, kidney, liver, lung or skeletal muscle, see page 17, lines 15-25); (d) it is therefore reasonable to conclude that the B1C3 receptor is probably involved in pain signaling and assays involving the isolated receptor should be useful in identifying agents that affect pain transmission. Using the criteria for credibility described above, Applicants submit that this reasoning is not seriously flawed and that there are no facts inconsistent with these assertions. It is therefore respectfully submitted that the utility requirement of patentability has been met.

II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

On pages 7-9 of the Office Action, the Examiner rejects all pending claims under 35 U.S.C. § 112, first paragraph. In part, the rejection is based upon an allegation that the application fails to adequately describe a use for the proteins and polynucleotides recited in the claims. However, since this aspect of the rejection depends upon whether the utility requirement under section 101 has been met, Applicants submit that it has been adequately addressed in the discussion above.[2]

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[1] See MPEP §2107.01

[2] In other words, if the utility requirement under section 101 has been met, then the requirement that the application describe how to use an invention under sec. 112 should also have been met.

The Examiner also rejects claims based upon the use of the transitional phrase "consisting functionally of." Since Applicants have eliminated this phrase from the claims as amended herein, it is submitted that this basis for the Examiner's rejection has been obviated.

Finally, the Examiner rejects claims containing the phrase "consisting essentially of" because this term encompasses not only proteins having exactly the same sequence as that of B1C3, but also proteins that contain insubstantial modifications in sequence as evidenced by their maintaining the same functional characteristics. The Examiner argues that, since Applicants have not described the exact structures falling within the scope of this definition, neither the written description nor enablement requirements of patentability have been met.

Applicants respectfully traverse this basis of rejection.

The Examiner appears to take the position that one of skill in the art must be able to recite all of the subject matter that falls within the scope of a claim in order for the written description requirement to be met. This is an inappropriate standard that could not be met by essentially any claim that uses either "comprising" or "consisting essentially" of as a transitional phrase. The more relevant questions are whether an application defines a genus (in this case a genus of polypeptides) sufficiently to distinguish other similar molecules in the art and whether the application has described a representative sample of the genus. As a practical matter, only polypeptides that encode a protein with a sequence that is highly homologous to B1C3 would raise a question as to whether they fall within the scope of the present claims and, in these cases, the issue could be resolved with a binding assay.[3] Thus, Applicants submit that the genus of polypeptides has been clearly defined. The question of whether a representative sample of the genus has been presented should be self evident. Applicants' claims only encompass B1C3 and proteins with insubstantial changes. Thus, the B1C3 protein presented in the application is representative of the genus because of the way that the genus has been defined. Applicants therefore submit that the written description requirement of patentability has been met.

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[3] Note that sphingosine-1-phosphate has now been identified as a ligand for B1C3 (see Glickman, *et al.* and Im, *et al.* cited above).

Similar considerations apply to the enablement requirement. The relevant test is not whether one can make and use the complete set of claim embodiments (*i.e.*, systematically set about synthesizing every single molecule). Essentially no claim using the "comprising" or "consisting essentially of" transition could meet such a standard. A more appropriate test is to ask whether any polypeptides can be identified that fall within the scope of the claims and that cannot be made and used. Given such a test and the routine nature of synthesizing polynucleotides that exists in the art, Applicants can see no basis for the Examiner's suggestion that the claims are not fully enabled.

III. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

On page 10 of the Office Action, the Examiner rejects claims under 35 U.S.C. § 112, second paragraph. Specifically, claims 1 and 6 (as well as their dependent claims) are rejected for using the terms "comprising" and "consisting functionally of" together. Applicants do not understand why these terms should be incompatible with one another or particularly confusing. Nevertheless, the claims have been modified so that there is now just one transitional phrase.

The Examiner also makes a separate rejection of claim 10 under 35 U.S.C. § 112, second paragraph. However, since this claim has now been cancelled, Applicants respectfully submit that the Examiner's rejection has been obviated.

IV. Rejection of Claims Under 35 U.S.C. § 102

On pages 10 and 11 of the Office Action, the Examiner rejects claim 1 under 35 U.S.C. § 102(b) as being anticipated by Nenonene, *et al.* (*J. Neurochem. 62:*1822-1834 (1994)). It appears that the rejection is based upon the argument that the phrase "except as existing in nature" includes crude membrane preparations that probably contain the B1C3 protein.

In response, Applicants have replaced the phrase "except as existing in nature" with the phrase "substantially purified." As defined in the present application, Applicants submit that this phrase does not include a relatively crude membrane preparation. Thus, the rejection has been obviated.

Conclusion

In light of the amendments and discussion above, Applicants submit that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims presently pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (202) 419-7013.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

By Michael A. Sanzo

Michael A. Sanzo
Reg. No. 36,912
Attorney for Applicants

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1801 K Street, N.W., Suite 401L
Washington, DC 20006-1201
Phone: (202) 419-7013